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Machine Learning for Early and Automated Diagnosis of Diabetic Retinopathy and Keratoconus

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***Abstract*—Eye diseases like Diabetic Retinopathy, Glaucoma, age-related macular degeneration, astigmatism and Keratoconus can cause blindness and lead to economic burden on the exchequer by way of treatment cost and manpower loss if not diagnosed and treated at the early stages itself. Screening camps are conducted by government and non-government organizations and private hospitals also. But in screening camps large number of people are to be evaluated and it causes fatigue in the qualified technicians involved. This might result in cases getting unnoticed. To avoid this, we need automated diagnosis with good accuracy, sensitivity and specificity. Recent developments in artificial intelligence, machine learning and deep learning have helped greatly in the automated diagnosis of medical conditions, with greater accuracy and without manual intervention. Of particular importance are the machine learning algorithms which are more adept in analyzing images. The development of devices like video Keratoscope, fundus imaging, Optical Coherence Tomography etc., resulted in large set of images which need to be studied, classified and labelled for future research work as well as for diagnosis. Machine learning plays an important role in analyzing the correlation between images of different classes. This paper reviews the literature on the applications of machine learning for early diagnosis of diabetic retinopathy, glaucoma and keratoconus, their limitations, future scope and also suggests a machine learning based approach for the diagnosis of diabetic retinopathy and keratoconus.**

Keywords— Machine Learning, Convolutional Neural Networks, Diabetic Retinopathy, Keratoconus, Early Diagnosis

I. Introduction

Diabetic Retinopathy (DR) is a leading cause of blindness among working-age adults. Early detection, which is critical for good prognosis, relies on skilled readers and is both labor and time-intensive. This poses a challenge in areas that traditionally lack access to skilled clinical facilities. Moreover, the manual nature of DR screening methods promotes widespread inconsistency. Automated techniques for diabetic retinopathy diagnoses are essential to solving these problems. Earliest signs of DR are red lesions, a general term that groups both microaneurysms (MAs) and hemorrhages Several methods for detecting red lesions have been proposed in the literature. Most of them based on characterizing lesion candidates using hand crafted features, and classifying them into true or false positive detections. Deep learning-based approaches, by contrast, are scarce in this domain due to the high expense of annotating the lesions manually. Keratoconus is a non-inflammatory disorder characterized by progressive thinning, corneal deformation and scarring of the cornea. The pathological mechanisms of this condition have been investigated for a long time. In recent years, this disease has come to the attention of many research centers because the number of people diagnosed with Keratoconus is on the rise. Keratoconus advances at varying rates and differently in each eye. Progression is generally more rapid, the earlier the age of onset. Keratoconus causes increasing blurriness and shortsightedness in vision, light sensitivity and halos and ghosting around light sources. Progression usually occurs to an age of around 40-45 years and then tends to stabilize. However, some progression may be experienced by persons 50 or older. On average, the most significant progression occurs in the first 15-20 years after the time of onset. Early Keratoconus, also called as Forme Fruste keratoconus has only very slight corneal distortion. It has little or no effect on the quality of vision and exhibits minimal or no progression. In moderate keratoconus corneal distortion increases and corneal changes typical of Keratoconus can be observed. As

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the vision quality with spectacles decreases, rigid gas permeable contact lenses become the option for better quality vision. In advanced keratoconus Substantial corneal distortion with moderate Keratoconic corneal changes, slight to moderate corneal scarring present. In severe keratoconus Dramatic corneal distortion, substantial corneal scarring and thinning. Early detection of keratoconus is essential for prevention of blindness or corneal surgery Existing methods provide good detection of advanced and severe Keratoconus, but lack in detection of early and moderate Keratoconus. With the advent of machine learning approaches, particularly the development of several architectures of Convolutional Neural Networks (CNN), the diagnosis of diseases has become easier and reliable.

II. Literature Review

Lam et al., employed an automatic Diabetic Retinopathy (DR) grading system capable of classifying images based on disease pathologies from four severity levels. A convolutional neural network (CNN) convolves an input image with a defined weight matrix to extract specific image features without losing spatial arrangement information. Different architectures have been evaluated first to determine the best performing CNN for the binary classification task. Then they have trained with multi-class models that enhance sensitivities for the mild or early-stage classes, including various methods of data preprocessing and data augmentation to improve test accuracy. The issue of insufficient sample size has been addressed using a deep layered CNN with transfer learning on discriminant color space for the recognition task.

Harry Pratt et al., have developed a network with CNN architecture and data augmentation which can identify the intricate features involved in the classification task such as micro-aneurysms, exudate and hemorrhages on the retina and consequently provide a diagnosis automatically and without user input. They have used increased number of convolution layers (13) to allow the network to learn deeper features. The first layer learns the edges while the deepest layer learns the features of classification. The network has been trained with the publicly available Kaggle dataset. The proposed method has demonstrated impressive results, particularly for a high-level classification task. On the data set of 80,000 images used the proposed CNN achieves a sensitivity of 95% and an accuracy of 75% on 5,000 validation images. Issues have been reported in making the network to distinguish between the mild, moderate and severe. cases of DR. The low sensitivity, mainly from the mild and moderate classes suggests the network struggled to learn deep enough features to detect some of the more intricate aspects of DR. The ongoing developments in CNNs allow much deeper networks which could learn better the intricate features that this network struggled to learn.

Kumar et al., have proposed a method for automated analysis and classification of the retina as DR or non-DR using two-field mydriatic fundus photography. The optic disc region is located by multi-level wavelet decomposition and recursive region growing from an automatically identified seed point. Blood vessels are extracted by applying histogram analysis on the two median filtered images. Red lesions are detected using three stage intensity transformation and white lesions from multi-level histogram analysis. The final classification of the retina as DR or non-DR is based on an aggregate of the lesions extracted from each image. The proposed method can be developed into a screening system and operated by a person without the diagnostic ophthalmology skills which eases the adoption of the system in the peripheral healthcare centres where there is scarcity of qualified ophthalmologists. The results show that the proposed method is able to screen out half of the non-DR cases and detect DR cases with high sensitivity, especially on higher grades of DR where severe and very severe retinas were detected with an accuracy of 93% & 96% respectively. For lower grades of DR, the accuracy is comparatively lesser at 84%, 62% and 50% for moderate, mild and very mild cases respectively. To improve the accuracy of detection of DR in all cases especially in the moderate to mild cases.

Ignacio et al., developed a method for red lesion detection based on combining both deep learned and domain knowledge. Features learned by a convolutional neural network (CNN) are augmented by incorporating hand crafted features. The authors have presented an ensemble approach that improves the features learned by a CNN by incorporating domain knowledge. The integration of both the deep learned and the hand-crafted features significantly improved results compared to using either approach separately. The proposed automated red lesion detection system could be integrated in a more general DR screening platform to improve the ability to detect DR patients. Moreover, a reliable DR likelihood can be complemented by an indication of the abnormal areas, allowing physicians to better identify the clinical signs of the disease and to have more comprehensive feedback from the system. Furthermore, incorporating other modules for detecting other pathological structures can eventually improve the reported performance.

Accardo et al., proposed a three-layered Neural Network with Back propagation training was used for classification as Normal N, Keratoconus KC and Others O. 10 indices were considered. Maps from single eye and both eyes of the same patient were considered for classification. Different combinations of layer sizes and learning rate parameters were considered. The proposed method achieved global sensitivity ranging from 81.7 to 94.1 and global accuracy of 92.9 to 96.4. The results vary with consideration of the single or both eyes. With single eye the accuracy level decreases. Also, the network was not able to classify subclinical or form fruste Keratoconus.

Souza et al., considered only one eye of each patient was randomly included in the study. 11 attributes from Orbscan II were used. SVM, MLP and RBFNN classifications were applied. The classifiers provided a good performance, and the area under the ROC curve of the support vector machine, multi-layer perceptron and radial basis function neural network were significantly larger than those for all individual Orbscan II attributes evaluated. The system provides detection of keratoconus and does not provide classification of stages of keratoconus. Different combinations of attributes need to be considered apart from the 11 attributes considered here. Data from both eyes of the patient to be considered.

Subramanian and Ramesh had employed Cat Swarm Optimisation to corneal topography images for improving the accuracy of the classification. Texture analysis using local binary patterns, local directional patterns and local optimal oriented patterns have also been applied to analyse and delineate prior to training the convolutional neural networks for training and classification.

Toutounchian et al., considered four groups of classifiers including Multi-Layer Perceptron (MLP), RBFNN, Neural Network (NN), Support Vector Machine (SVM) and Decision Tree (DT). The authors employed two sets of features. The first group (9) is the features obtained directly by Pentacam and the second group (3) is the features we obtained by analyzing the maps of topographical images acquired by Pentacam. Accuracy of nearly 100 for classification between Normal and Keratoconus eyes. However, the accuracy level decreases when classification done for all three cases (71 to 84%) i.e., normal, KC and Sub clinical KC.

Arbelaz et al., classified as abnormal, keratoconus, subclinical keratoconus, or normal, based on the data derived from both anterior and posterior corneal surfaces by support vector machine (SVM), a machine learning technique. In the distinction between normal and subclinical cases, precision increased from 57.4% to 78.8% when posterior corneal surface data were included in the analysis. While the precision for Normal, Abnormal and keratoconus eyes were nearly 98%, the precision of 78.8 % for subclinical can be improved by including more attributes and advanced classifiers.

Hidalgo et al., utilized Pentacam data for analysis. Dimensionality Reduction technique used to reduce the parameters to 22. Classification was done using SVM as Normal, Form Fruste KC, KC, Astigmatic and Post Refractive Surgery. Accuracy of classification between Normal and KC eyes was 98.9%. Sensitivity and specificity for KC detection were 99.1% and 98.5%, respectively. The accuracy is lower in the classification between Normal and Form Fruste KC (93.1%). The sensitivity is 79.1% and specificity is 97.9% for FF KC detection. The global accuracy for the classification task that involved the 5 groups was 88.8%, with a weighted average sensitivity of 89.0% and specificity of 95.2%.

Lavric et al., used KeratoDetect, an algorithm that was able to determine whether an eye is affected or not by keratoconus. It analyzes the corneal topography of the eye using a convolutional neural network (CNN) that is able to extract and learn the features of a keratoconus eye. The algorithm ensures a high level of performance, obtaining an accuracy of 99.33% on the data test set. This can assist the ophthalmologist in rapid screening of its patients. Topography of the same cornea would look different with the change in the steps of color. The smaller steps increase the sensitivity to pick up early keratoconus, but can falsely diagnose a normal cornea as keratoconic, whereas larger steps can miss out on the early changes. Hence, the topography should not be evaluated only based on the colors and the pattern.

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Subramanian and Ramesh had employed particle swarm optimisation for segmentation and index quantification of the corneal topography images. Convolutional Neural Networks was used for classification. Different pre trained models were used and the results compared.

Santos et al., have employed a customized fully Convolutional Neural Network, CorneaNet, for detection of Keratoconus. The network is used for segmentation of OCT images. The thickness maps of full cornea, Bowman layer, epithelial layer and Stroma are used and the segmentation speed considerably improved with the usage of the CorneaNet. Segmentation is faster using deep learning and the CorneaNet is able to segment both healthy and keratoconus images with high accuracy (validation accuracy: 99.56%). Reducing the number of features of the convolution layer decreased the validation accuracy by 0.1 whereas the increasing the number of features resulted in overfitting. Corneal maps provide an efficient alternative to the OCT scans to make effective use of deep learning architecture.

Lavric et al., (2020) have compared the performances of 25 different models in machine learning with an accuracy ranging from 62% to 94.0%. The best performance of 94% has been observed in a Support Vector Machine (SVM) that used eight corneal parameters which were selected using feature selection The proposed machine learning model was able to detect the early stages of the disease with an accuracy of 83%, while the classification between normal and keratoconus eyes achieved an accuracy of 93%. The proposed models were trained on corneal data from Casia instrument and are thus limited to this instrument. Classification accuracy decreases in cases of early Keratoconus.

Kuo et al., employed three pre-trained CNN models, namely, VGG16, InceptionV3 and ResNet152 for classifying the corneal topography images into Keratoconus and Normal. Accuracy levels of 0.93, 0.93 and 0.96 were obtained with the three models used. Different color scales are used and thus can be used with different image acquisition platforms like Pentacam, Galilei, Neidek etc., Posterior topographic maps only were used for classification and the anterior maps have not been used. The usage of both posterior and anterior maps has to be studied. Only two classes are discussed. Further classification into more classes including mild, moderate and severe are to be studied.

Lavric et al have evaluated the accuracy of keratoconus detection from corneal parameters including elevation, topography and pachymetry using machine learning algorithms. Elevation parameters provided the highest area under the curve (AUC) parameter of 0.99 in detecting normal from keratoconus cases and an AUC of 0.88 in detecting different severity levels when using only three most promising corneal parameters including minimum curvature radius, eccentricity of the cornea and asphericity of the cornea. Can be extended to more classes with corneal topography images also as input along with the elevation parameters.

III. Inference from literature review

Diabetic Retinopathy detection is done by analyzing the fundus images manually or automatically. Both processes depend on the identification of red and white lesions. Classification is done in various classes ranging from very mild to very severe. While all the methods have performed well for positive to severe cases, the performance accuracy is less for moderate, mild and very mild cases. There is scope for improving the accuracy for the moderate, mild and very mild cases by including evolutionary techniques in the feature extraction step. Algorithms including Back Propagation Neural Networks (BPN), Multilayer Perceptron (MLP), Support Vector Machines (SVM), Radial Basis Function Networks (RBFN), Decision Tree (DT), Convolutional Neural Networks (CNN) have been used for detection and classification of Keratoconus based on the corneal attributes/indices. Though hundreds of corneal indices are available from scans, only few, ranging from 9 to 21, are used for detection of keratoconus. The output and accuracy depend on the choice of the attributes/parameters. No fixed rule is available on the parameters to be used. The accuracy of the algorithms in the literature are better for classification between Normal and Keratoconus cornea. But when there is a need to classify/ distinguish between Normal & Sub-clinical Keratoconus or Sub-clinical & Keratoconus cornea the accuracy decreases. Only few efforts have been taken in the detection and classification of Keratoconus using topography elevation images Convolutional Neural Networks have been employed for detection of Keratoconus alone and not for classification,

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particularly not for the detection of sub-clinical Keratoconus. The proposed methodology is to use pre trained CNN models like VGGNet, ResNet and Google Net. The topography images are optimized for better results.

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